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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,657	RAMANATHAN ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response of April 14, 2004 is acknowledged. Claims 69-107 are pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 69-107 is acknowledged, as well as Applicant's election *with* traverse of a searchable compound as a further requirement of electing the invention; namely of PEG conjugated to a retro inverso protein or peptide. Applicant has argued that it would not be burdensome to search the entire scope of the claims. This is not found persuasive because the sheer number of different class/subclass searches of all the various compounds that are proposed as capable of use in the invention (see i.e. claim 103 ranging from peptides to toxins), would be unduly burdensome.

On 6/3/2004, the Examiner telephoned Robert Paradiso, Attorney for Applicant, to elect a single retro inverso protein or peptide. Following discussion, the Examiner agreed to search any one of SEQ ID NOS: 1-8 (retro inverso peptides), as drawn to the elected invention. PEG conjugated to any one of SEQ ID NOS: 1-8 thus constitutes the elected invention.

It is unclear at this point which claims are to be withdrawn as not being drawn to the elected invention, since the invention is unclear in light of the claim language. Thus, no claims were withdrawn at this time and all claims have been rejected, until the claims are amended to clearly define the invention and delineate which claims are or are not drawn to the elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112 1st Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the use of the invention as claimed and as elected.

The nature of the invention: The invention, as claimed, is drawn to a method of delivery of a therapeutic agent or a diagnostic agent comprising three components (1. polymer, 2. a therapeutic or diagnostic agent, and 3. a cell uptake promoter) and two embodiments thereof; namely, 1. a polymer and a cell uptake promoter both covalently bound to a therapeutic or diagnostic agent, or 2. a cell uptake promoter covalently and therapeutic or diagnostic agent both covalently bound to a polymer. However, Applicant has only elected two compounds as the invention, namely PEG (polymer) conjugated to a retro inverso peptide (i.e. elected SEQ ID NOS: 1-8).

The state of the prior art and the predictability or lack thereof in the art: The art teaches the conjugation of two compounds: namely a polymer conjugated to *one other compound* (more specifically *a therapeutic agent*) (see, for instance, the conjugation of PEG to Applicant's SEQ ID NO: 8 (WO 99/47173 (University of Medicine and Dentistry of New Jersey, see i.e. claims 1, 4, and 20)). Although art may teach two compounds conjugated to either

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification does not make clear the invention (i.e. claim 69). Specification para. 46 describes that "In some cases, the cell uptake promoter is a retro inverso peptide that acts as a transport enhancing moiety which increases therapeutic drug delivery into cells expressing receptors for the retro inverso peptide. *In some case[s], the transport enhancing moiety may also serve as a therapeutic agent itself.*" As discussed above, the claims describe that the invention MUST have 3 compounds conjugated together (PEG, a cell uptake promoter, and a therapeutic/diagnostic agent). However, the

specification describes that the transport enhancing moiety (assumed to be cell uptake promoter) MAY itself be the therapeutic agent. *If such is the case*, similar to Applicant's election of the invention (i.e. only two compounds conjugated, namely PEG conjugated to a retro inverso peptide (i.e. SEQ ID NOS: 1-8)), *then only two compounds are conjugated*: PEG and one of the retro inverso peptides. The specification has not clearly defined that there are three respective compounds conjugated together, as claimed.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to a method of delivery of a therapeutic agent or a diagnostic agent comprising three components (1. polymer, 2. a therapeutic or diagnostic agent, and 3. a cell uptake promoter) and two embodiments thereof; namely, 1. a polymer and a cell uptake promoter both covalently bound to a therapeutic or diagnostic agent, or 2. a cell uptake promoter covalently and therapeutic or diagnostic agent both covalently bound to a polymer. As claimed, in contradiction to the elected invention, it is not clear as whether one of skill in the art could carry out (or know whether he has carried out) the invention as claimed. Absent sufficient teachings in the specification to overcome the unpredictability of what constitutes the invention, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Therefore, others skilled in the art would be unable to practice the invention as claimed without undue experimentation and with a reasonable expectation of success.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 69-107 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 69-107 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed 4/14/2004. In that paper, applicant has stated that the elected invention is the conjugation of two compounds, PEG conjugated to a retro inverso peptide (i.e. namely SEQ ID NOS: 1-8), and this statement indicates that the invention is different from what is defined in the claim(s) because the claims (see claim 69) teach the conjugation of three compounds (1. polymer, 2. a therapeutic or diagnostic agent, and 3. a cell uptake promoter). It is suggested that the invention be clarified, including the limitation of the elected invention (i.e. PEG as found in claim 79 and SEQ ID NOS: 1-8, as found in claims 106-107).

Claim 69 (and dependent 70-107) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear whether the invention is a method for delivering a polymer conjugated to a therapeutic agent, the latter which is also conjugated to a cell uptake promoter; or a polymer conjugated to both therapeutic agent and a cell uptake enhancer? Applicant is asked to clarify which of the above is the invention, if either is the invention; or amend the claims commensurate in line with the election of the invention (two compounds conjugated; of which Applicant must further define whether the retro inverso protein (i.e. SEQ ID NOS: 1-8) is a therapeutic agent or a cell uptake promoter)?

Claim 106 recites the limitation "cell uptake promoter peptide" in line 2. There is insufficient antecedent basis for this limitation in the claim. Namely, it was not found in claims 103 or 69, to which claim 106 depends respectively, where there is antecedent basis for "cell uptake promoter peptide"; and it is thus unclear what this is (i.e. cell uptake enhancer species)?

Claim 107 recites the limitation "uptake enhancer" in line 2. There is insufficient antecedent basis for this limitation in the claim. Namely, it was not found in claims 104, 103 or 69, to which claim 107 depends, where there is antecedent basis for "uptake enhancer"; and it is thus unclear what this is (i.e. cell uptake enhancer)?

Conclusion

Since Applicant has only elected two compounds as the invention, namely PEG (polymer) conjugated to a retro inverso peptide (i.e. elected SEQ ID NOS: 1-8), as opposed to the conjugation of three compounds as claimed (see claim 69); it is unclear what the invention is and thus a meaningful search could not be carried out. A general search of the prior art revealed teachings of PEG conjugated to Applicant's SEQ ID NOS: 1-8 (i.e. the 'elected' invention, though not the claimed invention). For instance, WO 99/47173 (University of Medicine and Dentistry of New Jersey) teach the conjugation of PEG to Applicant's SEQ ID NO: 8 (see i.e. claims 1, 4, and 20). However, since it is unclear what the invention is based on the indefinite claim language, the above reference, among others, could not be applied as proper art rejection, since it is not known what constitutes the invention, based on the claims as drafted. Nevertheless, WO 99/47173 is prior art made of record and not relied upon, though considered pertinent to applicant's disclosure.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

MA
6/27/04

CHRISTOPHER R. TATE
PRIMARY EXAMINER